Solve ME/CFS Initiative

The SolveCFS Chronicle Spring 2015

I Am Bent But Not Broken

By Lindsey Beres

Growing up, I was involved in many sports, thrived in the intellectual forum of a classroom, and was frequently involved in both physical and cerebral collegiate clubs. I participated in a variety of charities throughout the community, had a flourishing social life, and enjoyed my fair share of fun-filled nights out. However, when I was 18, I started seeing numerous doctors for, what seemed like, unrelated, back-to-back recurring illnesses. By the time I was 19, I had been prescribed so many medications that I was hospitalized with kidney failure. It wasn't until I was 20 that I was diagnosed with Chronic Fatigue Syndrome.

My college years were spent at Northern Arizona University where, unfortunately, my true struggle with ME/CFS began. During my attendance, I was classified as a "disabled" student. To ensure I stayed enrolled, my mother, who is/was also my caregiver, attended classes in my absence. I finished college from a hospital bed and fell asleep during my graduation ceremony. At this time, my fatigue was severe enough that I was prescribed a variety of stimulants, as many ME/CFS/SEID patients are.

In my case, I've found that ME/CFS comes in waves. Two years of serious downtime is usually followed by two years of recovery. Each time my body goes through these waves, it comes out weaker than before. In earlier years, for each bodily system that began to fail, I was treated by a different specialist. I underwent alternative treatments such as brain mapping, sleep studies, physician-administered detoxes and psychotherapy, to name a few. It wasn't until I visited the BioCare Hospital in Mexico that I began to see an improvement in my overall functionality.

During my stay at BioCare Hospital, I went through a rigorous process to detox my body from all the traditional medications and environmental toxins that were present in my blood. Once my body was "clean," I was administered live embryonic stem cells from various animals like blue shark, bovine and tortoise. Six months after a three-week stay, my functionality raised from

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Lindsey Beres with her mother and caregiver, Nancy.

SMCI Washington D.C. IOM Report Briefing

On March 25, Solve ME/CFS Initiative President Carol Head delivered the following remarks—which have been edited here for space—to an audience of congressional staff members, federal officials and members of the media in Washington, D.C. A video recording of the full remarks can be found on the Solve ME/CFS YouTube channel, YouTube.com/SolveCFS.

Carol Head
President

I'm Carol Head, President of the Solve ME/CFS Initiative.

The publication of this IOM report regarding Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome is one of the most important days in the history of this illness. With its pre-eminent roster of scientists and experts, rigorous methodology and forthright conclusions, this is the substance we have long needed.

We're here today because it is time for our government to increase funding and support for this disease. We believe that the IOM report is a turning point in the history of ME/CFS for two key reasons.

First, the federal government has now clearly affirmed that this is a serious, physical disease, not a syndrome. For the million Americans who have long suffered with skepticism and lack of care, this is deeply affirming. And for the doctors, nurses and medical researchers, this definitively places this disease in its rightful place.

And therefore, there now exist no credible barriers to significantly increasing medical research funding for this disease that will lead to treatments and cures. Federal agencies and private medical research foundations now have a bright green light to move forward with substantial funding, commensurate with the number of Americans who suffer with this illness. The seriousness of this illness can now only be refuted by those who **choose** to be ignorant.

And at the same time, what didn't change when this report was published?

ME/CFS/SEID continues to be a complex, multi-system disease that is still at the very early stage of medical research and understanding. It can be reasonably debated whether this disease has aspects that involve the immune system, neurological system, genetics with epigenetic effects, viruses, bacteria, brain and spinal cord inflammation, and many other systems.

Rigorous research has been done into all those areas, with many compelling and interesting research results, but nothing yet definitive. And very few research

dollars have been available to replicate even the most compelling findings.

ME/CFS research is not yet far enough along to be of interest to pharmaceutical industry funders. Therefore, the potential sources of private funding are quite narrow and utterly insufficient to solve this complex disease.

And of course the other thing that has not changed, is that hundreds of thousands of patients continue to suffer. They are in pain, usually without a diagnosis, locked inside bodies and minds that no longer serve them well, almost always without a doctor who can help them, and with zero FDA-approved drugs or therapies.

There are hundreds of thousands who suffer intensely, whose once vibrant lives are lived in pain, with loss of ability to be self-sufficient and often with little hope for recovery.

We can and must change that.

The ME/CFS/SEID economic burden on our nation is significant. Our government has estimated a $17 to $24 billion economic burden, due to lost productivity, indirect and direct costs. What patients want most is to rise from their beds to be productive and lift the burden of care from others.

And there are so many who suffer. The IOM report estimates 836,000 to 2.5 million Americans suffer with this illness. The CDC has estimated 1 million Americans. And certainly there are millions upon millions around the world. This is NOT a rare disease.

Below is a chart showing 2014 NIH funding and prevalence for selected diseases.

As the chart shows on the bottom line, the 2014 NIH ME/CFS research spending budget totaled $5 million. And using the conservative CDC figure of 1 million patients, we see that that's $5 per patient annually.

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Disease	**Funding** *(in millions)*	**Number of Americans**	**Dollars spent per patient**
HIV/AIDS	$ 2,978	1,200,000	$ 2,482
Lupus	$ 99	350,000	$ 283
Multiple sclerosis	$ 102	400,000	$ 255
Autism	$ 188	3,500,000	$ 54
ME/CFS	$ 5	1,000,000	$ 5

Source: U.S. Institutes of Health. "Estimates of Funding for Various Research, Condition and Disease Categories (RCDC)." NIH, published March 7, 2014. http://report.nih.gov/categorical_spending.aspx

In this issue

Solve ME/CFS Initiative Hosts IOM Briefing in D.C.

On March 25, the Solve ME/CFS Initiative hosted a briefing in Washington, D.C., on the Institute of Medicine's report on Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome.

The briefing gathered congressional representatives, reporters, government officials and researchers in the ninth-floor rotunda at 101 Constitution Ave. More than 300 also viewed the event through a live webcast, which can be viewed on the Solve ME/CFS Initiative YouTube channel. Mary Sue Perpich, daughter of the late Gov. Rudy Perpich, helped to organize the event.

Speakers included:

- Dr. Ellen Wright Clayton, chair of the IOM committee on ME/CFS;
- Morgan Fairchild, actress, activist and former ME/CFS patient; and
- Carol Head, president of the Solve ME/CFS Initiative.

Ellen Wright Clayton, M.D., JD

Dr. Clayton began her presentation with some background on the landmark report and the unanimity the committee members experienced over the 18-month period. "It really was an amazing, dynamic process," said Clayton, who has chaired or co-chaired five other IOM committees. After providing an overview of the report's key recommendations, she offered her own thoughts about the next steps that need to be taken now that the committee's work is done.

"It is my sincere hope that people will use this report, which clearly demonstrates the seriousness of this illness, for advocacy with policymakers," she said. "It is time to fund more research into this disease's causes, defining subtypes and effective treatments. This will require stronger advocacy in—and outside—the government."

Clayton added: "We opened the door. The challenge now is to go through that door."

In her remarks, Solve ME/CFS president Carol Head made a forceful case for the need for dramatically more government funding for the disease (see related story). Through a series of slides, Head demonstrated that the funding for ME/CFS/SEID ranked 232 of the 242 National Institutes of Health spending categories in 2014.

"In actual dollars, the spending on ME/CFS is less than what our government spends on hay fever," Head said. She also showed that, given the prevalence of ME/CFS, the NIH funding is a mere $5 per patient, compared with $255 per multiple sclerosis patient and $2,482 per HIV/AIDS patient.

Given the disparity of federal funding, as well as the $17 to $24 billion economic burden on the country from ME/CFS, Head called for three actions:

1. Provide funding for biomedical research and studies commensurate with the disease burden. Head said that based on disease prevalence, NIH funding should be roughly $250 million annually.
2. Resolve the organizational and institutional barriers within the federal departments. "We need a strategic and tactical plan and commitment to solving this disease across agencies, perhaps even an ME/CFS czar."
3. Accelerate education of the nation's medical professionals since "patients cannot wait."

Morgan Fairchild led off her remarks with a question. "I know a lot of you are wondering, why is Morgan Fairchild talking about this disease?," she said. "It's because Morgan Fairchild has had this disease."

Fairchild explained that she had always been interested in science and research

Morgan Fairchild and Carol Head meet with representatives from the offices of Congressman Joe Kennedy and Sen. Harry Reid after the briefing.

and had read a fair amount about ME/CFS in the 1980s. In 1989, after returning to L.A. from a movie shoot in Portland where it had been cold and rainy, she went to see her doctor who diagnosed her with Chronic Fatigue Syndrome. "Suddenly, CFS wasn't just a fascinating case study; I was one of the cases," she said. While Fairchild didn't suffer from fatigue at the time of diagnosis, she says, "When it hit me, it hit me like a ton of bricks."

She was fortunate on a number of fronts: She had a mild case, she was diagnosed early, and she had a doctor who didn't think she was "nuts."

Fairchild said she learned how to pace herself and save herself for her work, which was manageable since movies require work in spurts with long down times in between, when she could rest. While the brain fog made it harder to learn her lines—something that had always come easily to her—she "was able to muddle through and keep making a living." She knows this is not the case for most ME/CFS/SEID patients.

"I was very lucky, Carol was very lucky," she said. "We got past it."

Fairchild says she's committed to making the path easier for others.

"Real pain and devastation exist because of this disease," she told the in-person and webcast audiences. "We need the powers that be to give us focus and funding because, honey, the science ain't free." ■

To sign up for our monthly e-newsletter, Research1st, go to:

SolveCFS.org/newsletters

Update on Biovista Project

As previously reported in the *Chronicle*, in 2012 the Solve ME/CFS Initiative awarded a grant to Biovista, a biotech firm with expertise in repurposing old drugs for new uses. Biovista used its state-of-the-art computational platform to evaluate more than 90,000 compounds together with 25,000 clinical outcomes and the more than 6,000 biomedical publications on ME/CFS. The approach looked for correlations between drugs, the way they interact with the body and ME/CFS symptoms. The goal was to find one or more compounds that could be repurposed to safely and effectively treat ME/CFS/SEID.

Biovista's analysis uncovered two drugs, which could be used in combination to treat ME/CFS patients. Because the drugs had not been tested together, a clinical trial was the next step to determine the safety and efficacy of them to treat ME/CFS/SEID. Biovista is currently raising funds and looking for partners to conduct a clinical trial on this two-drug combination in ME/CFS/SEID patients. We will continue to keep you updated on this project, which could have important implications for patient treatment options. ■

SMCI Research Plan: The Big Picture

SMCI is now in its first year of a five-year research plan, which takes a comprehensive approach to solving ME/CFS/SEID. The plan, developed in 2014, reflects the bioinformatics approach, which is the science of collecting and analyzing complex biological data. The overarching aim is to define ME/CFS through the powerful combination of patient experiences and data from multiple research studies. Under the leadership of the Research Director, SMCI will continue to collaborate with other investigators as it leads this comprehensive research project, which is based on a three-step approach:

1. Recruit and engage a large community of ME/CFS/SEID patients to participate in research and contribute health information and biological samples through our well-established SolveCFS BioBank™.
2. Work with best-in-class scientists using proven technology to generate molecular data about how genes, viral exposure, immune response and many other factors contribute to ME/CFS/SEID.
3. Collect, integrate and analyze experiential and health information from patients along with their molecular data to define ME/CFS and its subtypes.

By systematically generating, collecting, integrating and analyzing this information, we will move ME/CFS from a medically unexplained disease, to a disease with molecularly defined subtypes. This infrastructure is critical for developing robust diagnostics and personalized treatments.

Expected SMCI Research Project Outcomes

- Defining what ME/CFS/SEID is and breaking it down into its various subtypes at a symptomatic, physiological and molecular level
- Participation by thousands of ME/CFS patients and healthy subjects to finally be able to conduct unbiased research on this disease
- Understanding biologic systems that have gone awry in ME/CFS, identified by subtype; for example, viral versus endocrine or a combination
- Information for patients about their disease subtype and biology
- Creation of a permanent, flexible research infrastructure and resources, including an expanded SolveCFS BioBank™
- A robust evidence base to drive objective diagnosis and targeted treatments

This five-year project is the next logical step in the long-standing work of the Solve ME/CFS Initiative to improve the lives of the millions who suffer from this devastating disease. ■

To support the Solve ME/CFS Initiative's research efforts, make a gift using the enclosed envelope or contribute online at SolveCFS.org/donate

Competitive Award Recognizes Importance of Solve ME/CFS Initiative Research

The Solve ME/CFS Initiative is launching one of the most exciting research projects in the history of our organization.

In the fall of 2014, SMCI was invited to submit a proposal to the Dr. Ralph and Marian Falk Medical Research Trust. The competition was open to any U.S.-based research team; almost 250 proposals were received. The Solve ME/CFS Initiative was one of only a handful of projects to receive the award, which is clear testament to the quality of our organization's research program.

The $500,000 in funding received from the Falk grant will help build on the work of Dr. Patrick McGowan from the University of Toronto, who published a study in 2014 of his SMCI-funded research. McGowan's work used blood cells from the SolveCFS BioBank™, which showed there were differences in the epigenetic modifications to the DNA of 12 people with ME/CFS vs. 12 healthy controls. Epigenetics refers to patterns of change in gene expression—not the gene itself—that occur in response to things such as nutrition, infection, and physical and mental trauma that are not genetic factors. Dr. McGowan's 2014 results also showed significant differences in epigenetic modification to genes involved in the body's immune response.

Patrick O. McGowan, PhD
Assistant Professor, Department of Biological Sciences, University of Toronto

In this year's new study, Dr. Lucinda Bateman and her team at the Fatigue Consultation Clinic in Salt Lake City, Utah, will enroll 150 new patients and 150 matched controls over the next four months. Blood samples will be drawn from each participant and sent to the SolveCFS BioBank™ to be processed. A small portion of each sample will be shipped to Dr. McGowan immediately, while the remainder of the blood samples from study participants will be stored in the SolveCFS BioBank™ for future research.

Dr. McGowan's team will sort the blood cells into different types and extract DNA from specific cell types of interest—especially immune cells—based on his first study results. The data from this study will be collected by the end of October and analyzed to see if it confirms Dr. McGowan's earlier findings of epigenetic modification in people with ME/CFS/SEID vs. healthy controls. Final results are expected by year-end.

The research has a host of potential implications. An abnormal pattern of epigenetic modification in immune cells could be shown to be responsible for different immune response in people with ME/CFS. Abnormal epigenetic patterns potentially could be used for molecular diagnosis of ME/CFS/SEID or as drug targets for therapies. These patterns might also be relevant in selecting people for future clinical trials. The findings could be integrated with other studies—like the one published by Hornig-Lipkin earlier this year (see Page 17)—which show specific immune responses that are being altered in ME/CFS.

Given the number of subjects enrolled in this study, the results are expected to either confirm or refute the results from Dr. McGowan's earlier study and may uncover additional patterns that are currently unknown.

Regardless of the final results, the outcome of this study will help expand understanding of ME/CFS/SEID and guide where the Solve ME/CFS Initiative should focus its future research investments. SMCI is supplementing the cost of the study with $150,000 of its own funds. ■

Redefining an Illness

by Suzanne D. Vernon, PhD
SMCI Scientific Director

On Feb. 10 of this year, the Institute of Medicine (IOM) issued its long-awaited report on diagnostic criteria for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) titled, "Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness." This 304-page landmark report is remarkably thoughtful, highly informative and an accessible evidence-based document that, among other things, succeeded in giving medical providers a much-needed framework for diagnosing ME/CFS (SEID).

There has been much discussion on the diagnostic criteria put forth in the IOM report, and debate on how this may effect clinical practice and research. It is important to begin with clarifying what is meant by "case definition" and "diagnosis," given that a research case definition and a clinical case definition are different.

Research case definition is an epidemiological tool used to establish whether a patient can be linked to an outbreak and to determine the number of people in the affected population—or "cases"—involved in an outbreak. Epidemiology is the science that studies the patterns, causes and effects of health and disease conditions in a specific population. Case definitions are used in research to identify biomarkers and causes of diseases. It is not recommended that case definitions be used to guide clinical practice. Case definitions are simple and practical and are formulated to include the following components:

- Time—A period of time "cases" are associated with an outbreak
- Place—Limiting "cases" to a geographical location
- Person—Personal characteristics, like age and gender, as well as clinical and laboratory criteria that are hallmarks of the illness

Diagnosis is the process used by a medical provider to explain what may be causing an individual's malady, which often presents as nonspecific symptoms and signs. Many medically unexplained diseases, like ME/CFS, do not have objective diagnostic tests, which makes diagnosis challenging. Medical providers use many of the following types of information to make a diagnosis:

- Intake history—the events that preceded the visit to the doctor
- Medical history
- Family history
- Physical examination
- Diagnostic tests—blood tests, imaging procedures, etc.

Perhaps the biggest difference is that "research case definition" deals with populations of patients, and "clinical case definition for diagnosis" focuses on the individual.

There are currently no diagnostic laboratory abnormalities or clinical tests that can be used to diagnose ME/CFS/SEID. The IOM committee was charged with developing evidence-based clinical diagnostic criteria for ME/CFS. In other words, what could the IOM committee confidently recommend that medical providers could use to diagnose ME/CFS in an individual who visits their office? To determine these recommendations, the IOM committee did not limit themselves to the peer-reviewed medical literature. They also drew upon the extensive input from the patient community and reviewed and evaluated unpublished data. The committee developed a process or diagnostic algorithm that providers could use to make an ME/CFS/SEID diagnosis.

The flow diagram on Page 9 is the streamlined and systematic approach using specific diagnostic criteria that the IOM committee recommended. The simpler and clearer the diagnostic criteria, the more likely it is to be used by doctors and nurses, many of whom lack familiarity with the disease.

ME/CFS has been poorly defined, which means that diagnosis is difficult. This is not uncommon for a multisystem, complex disease, with symptoms that appear in other illnesses as well and can be difficult to measure objectively. With new, clear diagnostic criteria as put forth by the IOM committee, diagnosis is far less complicated

and more readily deployed in the clinical setting. The new diagnostic criteria include the following three cardinal symptoms of ME/CFS/SEID:

Diagnosis requires that the patient have these three symptoms:

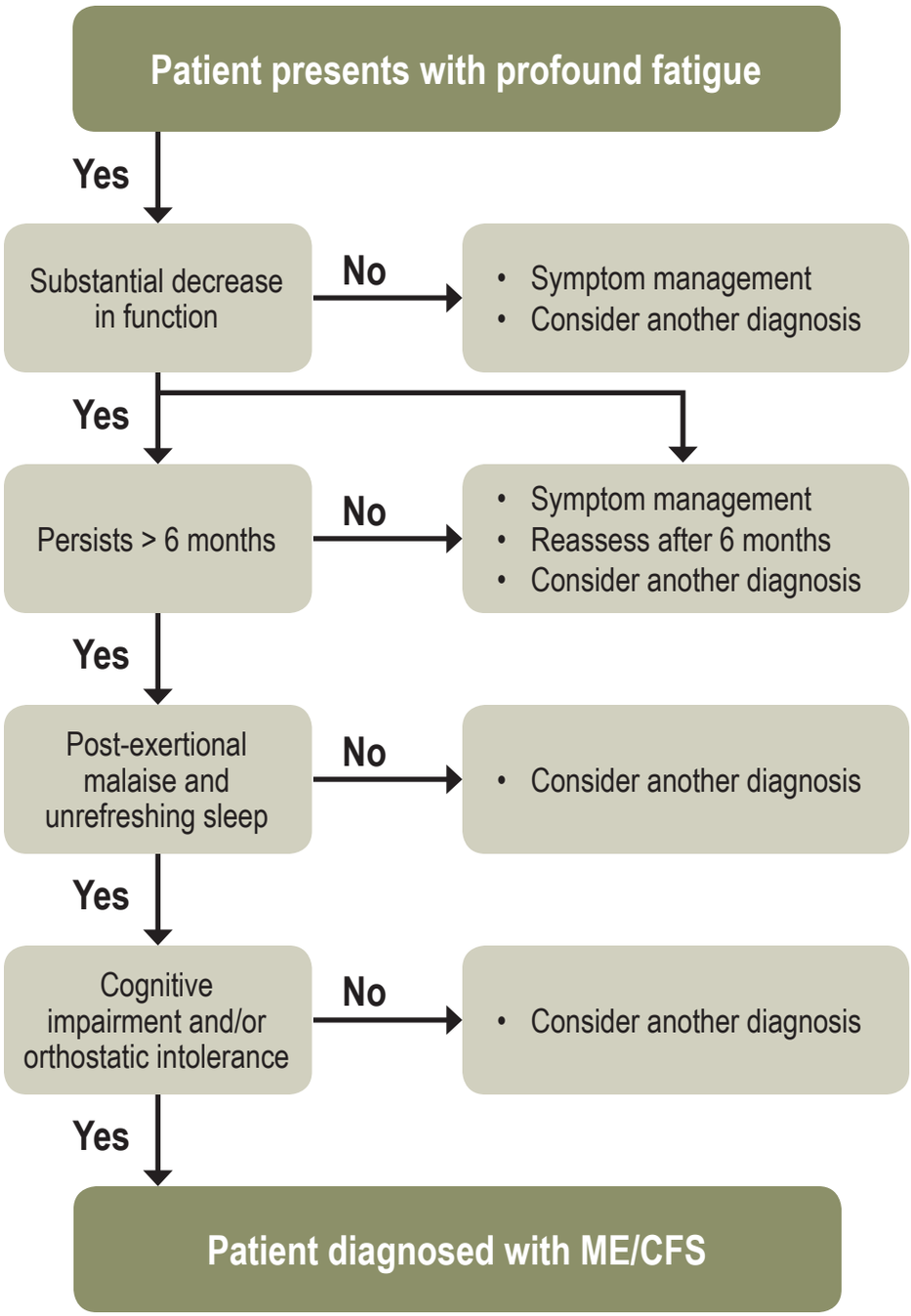
1. A substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social or personal activities that persists for more than six months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest; and
2. Post-exertional malaise*; and
3. Unrefreshing sleep*.

At least one of the two following manifestations is also required:

1. Cognitive impairment* or
2. Orthostatic intolerance

*Frequency and severity of symptoms should be assessed. The diagnosis of ME/CFS/SEID should be questioned if patients do not have these symptoms at least half of the time with moderate, substantial or severe intensity.

Insititute of Medicine Recommended Diagnostic Criteria



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Redefining an Illness (continued from Page 9)

IOM Diagnosis Factor One

The first recommended diagnostic criteria examines the impact of fatigue on function. To illustrate the impact of fatigue on function in ME/CFS/SEID, the IOM committee compared vitality across a number of diseases. Vitality is one of the scales on the SF36—a standardized assessment instrument—that assesses energy and fatigue by asking for responses to four questions: 1. "How much of the time during the past four weeks did you have a lot of energy?;" 2. "...have you felt full of life?;" 3. "…did you feel worn out?;" and 4. "…did you feel tired?" The comparison of responses between those who have ME/CFS/SEID and who do not clearly illustrated the profound effects the disease has on vitality. I've created the table below to show you some of the vitality scores for healthy people, a few diseases and ME/CFS.

Other research using the SF36 has shown physical activity and social functioning are also impacted in ME/CFS. While the IOM noted the extensive use of the SF36 in research, it did not recommend it as a tool for doctors to use because it is complicated to score. However, it seems reasonable that an app could be developed for use in a doctor's office (there is currently an SF36 app in the iTunes App Store, but it is not in English).

IOM Diagnosis Factor Two

PEM is defined as an exacerbation of some or all of an individual's ME/CFS/SEID symptoms that occurs after physical or cognitive exertion and leads to a reduction in functional ability. Patients have long known that PEM is a characteristic feature of their disease and individuals have described it as "crash," "debility" and "hitting the wall." This illustrates how variable the experience of PEM is for ME/CFS patients.

While there are currently no standardized, objective measures of PEM, this is an important area of research, and studies are being conducted to identify PEM biomarkers. Until PEM can be objectively measured, doctors must rely on eliciting information from the patient. The IOM recommended that clinicians use the following questions to diagnose PEM:

- What happens to you after you engage in normal physical or mental exertion?
- How long does it take you to feel bad?
- How long does it take to recover from physical or mental effort?
- If you go beyond your limits, what are the consequences?
- What types of activities do you avoid because of what will happen if you do them? (Consider asking patients to keep a diary for a week or two.)

These are actually very good questions that do not bias a patient toward a particular symptom—fatigue or pain—but rather elicit the patient's

	Vitality Score
Healthy people	60-70
Congestive heart failure	29
Chronic hepatitis C patients	48
Rheumatoid arthritis	43-52
ME/CFS	15-20

own, individual experience. Responses will give the doctor the information on exertion intolerance needed to make a diagnosis of ME/CFS and provide the symptom management and supportive care needed.

IOM Diagnosis Factor Three

Sleep is essential to recovery and rejuvenation of every system in the body—immune, nervous, muscular, etc. It is the time when our body builds up and replenishes the molecules that are essential for the body to function when awake. Yet sleep disorders and diseases are very common, and almost everyone experiences disturbances including problems falling and staying asleep, waking up early, sleeping all day and being awake all night. We now know that left untreated, severe and chronic sleep disorders increase the risk of developing other chronic diseases such as heart and cardiovascular diseases.

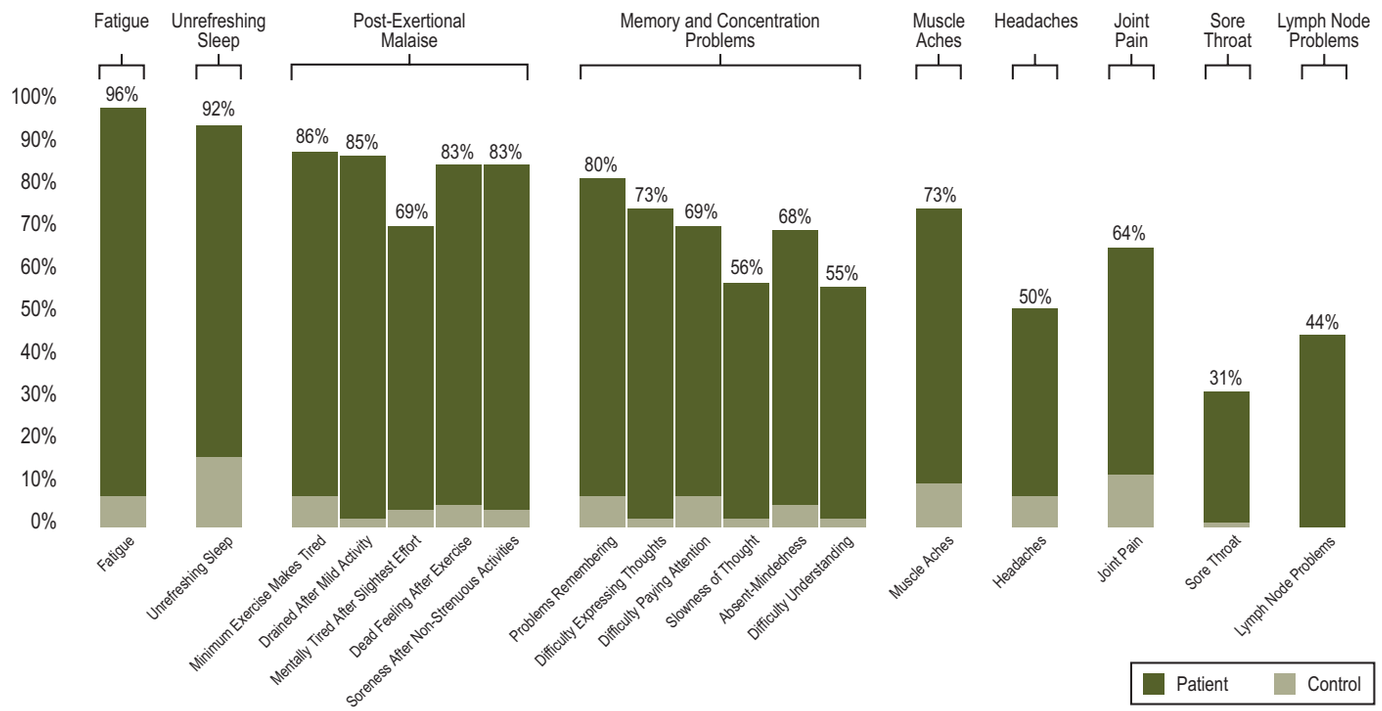
Unrefreshing sleep, which is described as "feeling as tired upon waking as before going to bed," is one of the most common symptoms reported by ME/CFS patients. The graph below is from a study conducted by DePaul University with SolveCFS BioBank™ participant responses to the DePaul Symptom Questionnaire. The dark green portion of each bar corresponds to responses from ME/CFS patients; the light green portion from healthy control patients. Unrefreshing sleep and fatigue are the two most common symptoms in more than 90 percent of ME/CFS/SEID patients.

The IOM committee relied largely on patient-reported information to decide on unrefreshing sleep as one of the ME/CFS diagnostic criteria. After a review of the data and peer-reviewed biomedical evidence, they concluded:

> *"Despite the absence of an objective alteration in sleep architecture, the data are strong that the complaint of unrefreshing sleep is universal among patients with ME/CFS when questions about sleep specifically address this issue. While PSG (polysomnography) is not required to diagnose ME/CFS, its use to screen for treatable sleep disorders when indicated is appropriate. Diagnosis of a primary sleep disorder does not rule out a diagnosis of ME/CFS."*

Continued on Page 12

Percentage of CFS Patients and Controls with Frequency and Severity Scores >=2 (Fukuda Symptoms)



Redefining an Illness (continued from Page 11)

The IOM committee recommended that medical providers ask about unrefreshing sleep when taking the medical history diagnosis. Example questions that can be asked include:

- Do you have any problems getting to sleep or staying asleep?
- How do you feel in the morning or after you've slept?
- Do you need too much sleep?
- Do you need to take more naps than other people?

Questionnaires are available to determine the frequency and severity of unrefreshing sleep, including the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale. Certain medications, diet and behavioral changes can be used to treat sleep disorders and have been shown to help ME/CFS symptoms.

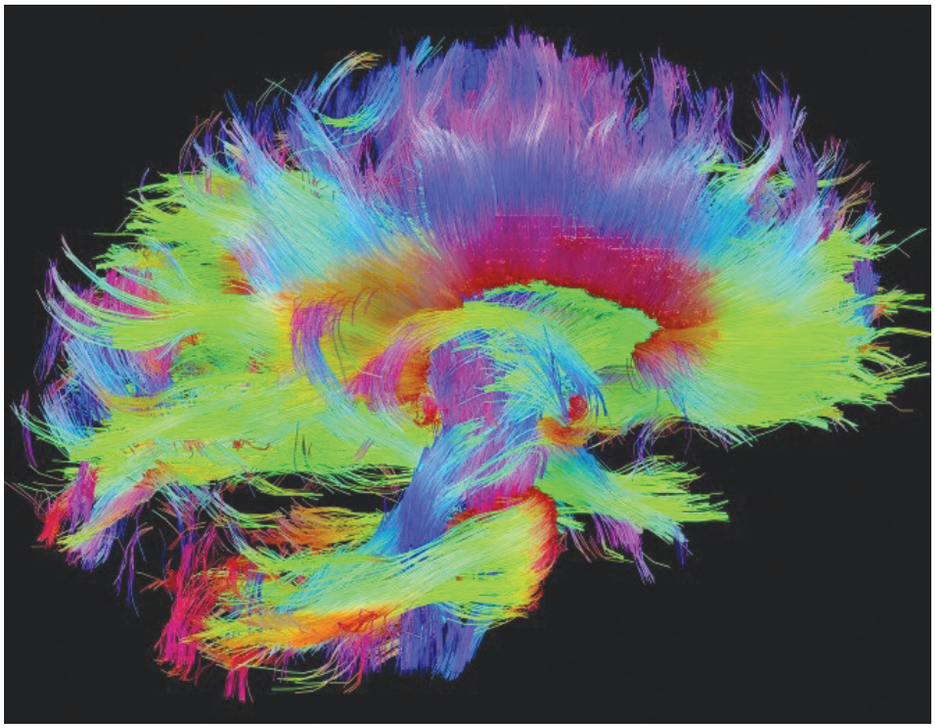
IOM Diagnosis Factor Four

Apart from fatigue, post-exertional malaise and unrefreshing sleep, diagnosis requires that a patient also must have either cognitive impairment and/or orthostatic intolerance. Cognition is a suite of interrelated conscious and unconscious mental activities and processes including learning, memory, attention and processing speed. At one time, it was thought that these abilities and processes were located in discrete regions of the brain. With the help of powerful imaging technologies we now know that the brain is more like a highly sophisticated, multidimensional circuit board with wires traversing the brain to help ensure coordinated neural communication and function.

Patients describe the effect of ME/CFS on their brain as "brain fog," "confusion," "disorientation," "hard to concentrate, can't focus," "inability to process information," "inability to multitask," and "short-term memory loss."

Neuropsychological research, which is research aimed at understanding the structure and function of the brain in people with disease, has shown that the cognitive impairment experienced by ME/CFS/SEID patients is due to slowed information processing. Processing speed is defined as, "The rapidity with which a cognitive operation is undertaken successfully. Although this is usually related to the speed of information processing, it may also apply to the speed of retrieval. Processing speed affects performance in many tasks and is operationally related to reaction time." Impairment of processing speed is a common feature of other neurological diseases.

The IOM committee concluded that there was sufficient evidence to show



"White Matter Fibers, HCP Dataset Red Corpus Callosum," courtesy of the Laboratory of Neuro Imaging and Martinos Center for Biomedical Imaging, Consortium of the Human Connectome Project: www.humanconnectomeproject.org

that slowed information processing was common in patients with ME/CFS/SEID and recommended that doctors ask the following questions to assess processing speed:

1. Do you have problems doing the following activities:
   - Driving
   - Watching a movie
   - Reading a book or magazine
   - Completing complex tasks under time constraints
   - Following or participating in conversation, doing more than one thing at a time?
2. Compared with before your illness, how is your performance at work or school?

The committee indicated neuropsychological testing could be used to provide objective data on slowed information processing. It should be noted that a neuropsychologist or someone with the appropriate expertise should administer formal neuropsychological tests. Physicians could also use questionnaires to obtain information on cognitive impairment, including the Wood Mental Fatigue Inventory, Checklist Individual Strength Questionnaire, and The Cognitive Failures Questionnaire.

Orthostasis means standing upright. Orthostatic intolerance is "the development of symptoms while standing upright that are relieved by lying down." The research evidence was strong that symptoms of orthostatic intolerance are common in ME/CFS patients. The IOM committee concluded the following:

> *"Sufficient evidence indicates a high prevalence of orthostatic intolerance in ME/CFS, as measured by objective heart rate and blood pressure abnormalities during standing or head-up tilt testing or by patient-reported exacerbation of orthostatic symptoms with standing in day-to-day life. These findings indicate that orthostatic intolerance is a common and clinically important finding in ME/CFS."*

The IOM committee recommended that doctors ask the following questions:

- How do you feel when you have been standing still for more than 1-2 minutes?
- What happens to you after you get up rapidly after sitting for a long time?
- How long can you stand before feeling ill? For example, can you do the dishes? Can you stand in line for a bus or movie? Are you able to grocery shop or be at a mall for more than a few minutes? Can you take a hot shower or hot bath without feeling tired and lightheaded? Do you have to sit down or lie down after a shower? Have you fainted or felt like you were going to faint while standing?
- Do these symptoms get worse in hot weather?
- Do you study in a reclining or prone position?
- Do you prefer to sit with knees to your chest or legs under you?

Next Steps

The IOM's comprehensive report on diagnostic criteria for ME/CFS/SEID is extraordinary both for its breadth and its depth. The report is a huge leap forward in helping patients get diagnosed, which in turn will create more potential research participants. As the IOM committee found, "remarkably little research funding has been made available to study the cause of ME/CFS" and "large studies that include individuals with diverse symptoms are needed" to get a clearer picture of the disease. In the months and years ahead, the historic IOM report will help to inform the patient-centered research SMCI conducts through our Research Institute Without Walls and our SolveCFS BioBank™. ■

Download the Institute of Medicine's ME/CFS Clinician's Guide at solvecfs.org/research and share it with your healthcare provider

Carol Head Comments from SMCI Washington D.C. Briefing

(continued from Page 3)

On a percentage basis per patient, we see that spending on ME/CFS per patient is:

- 2% of spending per patient on lupus;
- 2% of spending per patient on MS; and
- 9% of spending per patient on autism.

NIH publishes a list annually showing its spending on various medical challenges and diseases. In 2014, the ME/CFS research budget ranked 232 out of 242 diseases funded by NIH, at $5 million for the year.

And in actual dollars, the spending on ME/CFS is less than what our government spends on hay fever.

Understanding the economic burden on our nation, the suffering of our citizens and the new disease validation with the IOM report, what now?

Carol Head speaking in Washington, D.C., at the IOM Report Briefing

With this new report, there are many actions that can be taken to do right by patients and their families. I ask only three:

First, provide funding for biomedical research and studies commensurate with the disease burden.

That is, use research dollars to aggressively advance understanding of disease etiology, pathology, diagnostics, treatment and natural history in patients across the spectrum of disease severity, patient age, race and socioeconomic status.

The math is straightforward based on the chart. Based on disease prevalence, NIH funding would be roughly $250 million annually to be comparable to spending on lupus or multiple sclerosis.

At $5 million in research spending and the estimate of national economic impact of $17 to $24 billion, the economic cost to our economy is more than 4,000 times our government's current spending on ME/CFS/SEID. I challenge the Office of Management and Budget or NIH to find a more effective use of incremental federal funds than to support research into ME/CFS.

This is a medical problem that can be solved.

Our second request: Resolve the organizational and institutional barriers within the federal departments. We need a strategic and tactical plan and commitment to solving this disease across agencies, perhaps even an ME/CFS czar.

One clear immediate change is to change the location of this disease from the Office of Research on Women's Health. This disease must be housed within an NIH institute with budgets and substantial funding authority, perhaps NIAID (Immunology) or NAIDS (Neurology). This disease needs an institutional home that is appropriate and can advocate for dollars and action.

And our third request, as called for in the IOM report, is to accelerate education of our nation's medical professionals. Patients cannot wait.

This means, among other things, acting on the IOM report's recommendation to disseminate information about the disease to medical schools and working professionals. This is eminently doable with appropriate funding and a thoughtful implementation plan.

In conclusion, so many people have suffered for so long without medical help or compassion. Along with a million other Americans and their loved ones, I fervently believe this is the beginning of the end of this deplorable tragedy that is not worthy of the American people.

This definitive IOM report has once and for all declared that we must

commit to funding research to eradicate this dreadful disease. Now there can be no excuses.

No excuses from our nation's health agencies that haven't funded research at a level commensurate with the economic burden it places on our nation's economy, or in comparison with other diseases.

And no excuses from anyone—doctors, friends, coworkers or family—who dismiss the devastating suffering of a million or more of our fellow Americans.

Our society's understanding of this disease is where, say, MS or autism was 30 years ago—poorly understood, largely dismissed, with skepticism about the cause.

Such has been the inhumane dismissal of those who suffer now with ME/CFS. One day the skepticism about ME/CFS and the poor treatment of those who suffer will be equally unimaginable to everyone.

With this highly credible, scholarly IOM report, now is the time to Solve ME/CFS.

Thank you. ■

To view the PowerPoint presentations from the briefing, go to:

www.solvecfs.org

Suzanne D. Vernon Steps Down from Scientific Director Post

Suzanne D. Vernon, PhD
SMCI Scientific Director

Eight years after joining the Solve ME/CFS Initiative (SMCI), Suzanne D. Vernon, PhD, will be stepping down as Scientific Director in late June. She will continue with the organization in a consultancy role for an extended period. SMCI has begun an international search for a Research Director.

As the organization's first Scientific Director, Vernon played a key role in transforming SMCI into a patient-centered research organization—one that translates donor-funded research into tangible results and progress. Shortly after joining SMCI in 2007, Vernon tapped into her professional network to spark interest in ME/CFS/SEID research. Her efforts resulted in more than 10 new investigators becoming engaged in ME/CFS research. "ME/CFS is a blank slate, and for scientists this represents a great opportunity for discovery," says Vernon.

During her time with the organization, Vernon established the SolveCFS BioBank™, which is one of the few biobanks focused on ME/CFS. "Our SolveCFS BioBank™ puts patients as partners in the research pipeline," says Vernon.

SMCI's long-term research program will continue on course, benefitting both from the continued perspective of Dr. Vernon, as a consultant, as well as the perspective of a new Research Director. With the added expertise of the organization's Research Advisory Council, SMCI's research program continues to gain authority and influence.

Vernon is excited about the opportunities that are ahead of her. She is considering a return to her infectious disease roots, as well as embarking on quantified self research in the chronic disease space.

"Suzanne has made an indelible contribution not only to our organization, but also to the field of ME/CFS/SEID research broadly," says Solve ME/CFS President Carol Head. "Her efforts will continue to bear fruit for many years to come."

Head adds that this is an exceptional time for research into ME/CFS/SEID, given the impetus of the Institute of Medicine report. "We look forward to building on the current research momentum, which is beginning to bring clarity to this complex, insidious disease," Head says. ■

SolveCFS BioBank™: Fueling Patient-Centered Research

The SolveCFS BioBank™ was approved by the Genetic Alliance for operation in April 2010. The BioBank launched through a partnership with GlaxoSmithKline (GSK) and several of the top ME/CFS expert clinicians in the United States. This partnership generated a precious inventory of samples from patients diagnosed by ME/CFS clinical experts as well as healthy control samples. The partnership also attracted new investigators into ME/CFS/SEID research.

Several of these investigators either have published or are preparing manuscripts on their research that use the SolveCFS BioBank™ samples; others have submitted applications to the National Institutes of Health based on these preliminary results. One of the most recent papers was published in the highly prestigious journal, *Brain, Behavior and Immunity*. The paper, "Anti-Neural Antibody Response in Patients with Post-Treatment Lyme Disease Symptoms versus those with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome," found that antibodies to central nervous system proteins were different between ME/CFS patients and post-treatment Lyme disease patients. This research points to diagnostic methods to distinguish between these two clinically similar diseases.

Our intention is to grow the SolveCFS BioBank™ into the most sought after resource for ME/CFS/SEID research in existence, and to do that, we need your help. Please consider enrolling as a participant and encourage your friends and family members who do not have ME/CFS to enroll as healthy controls. Go to solvecfs.org/biobank for more information on eligibility requirements. ■

McDermott Will & Emery

Thank You

The Solve ME/CFS Initiative would like to extend our sincere thanks to the international law firm McDermott, Will & Emery, which has provided our organization with legal services pro bono. As a nonprofit with limited resources, MWE's contribution is invaluable in helping us to make well-informed decisions that impact the health of our organization and the work we are doing on behalf of the ME/CFS community.

New Research Studies Confirm Biological Basis to ME/CFS

Two new studies by researchers at the Center for Infection and Immunity at Columbia University's Mailman School of Public Health provide further evidence of the biological underpinning of ME/CFS/SEID.

In the first study, researchers used immunoassay testing methods to determine the levels of 51 biomarkers in blood plasma samples collected, which included 298 ME/CFS patients and 348 healthy controls.

Researchers discovered that patients who had had the disease for less than three years had increased amounts of several different types of immune molecules—known as cytokines—compared with both ME/CFS/SEID patients who had had the disease longer than three years and with healthy controls.

"This study delivers what has eluded us for so long: unequivocal evidence of immunological dysfunction in ME/CFS and diagnostic biomarkers for disease," says senior author W. Ian Lipkin, MD.

According to the Mailman School, the evidence showed a significant association with a cytokine called interferon gamma, which has been previously linked to the fatigue that follows many viral infections, including Epstein-Barr virus. Many patients report suffering from a flu-like illness and never fully recovering before they begin their decline into ME/CFS/SEID.

The study indicates that the immune system of ME/CFS patients goes into overdrive in the early days of the disease and then gets stuck there before burning out and dropping off to near-normal levels after being sick longer than three years.

"It appears that ME/CFS patients are flush with cytokines until around the three-year mark, at which point the immune system shows evidence of exhaustion and cytokine levels drop," said Dr. Mady Hornig, the study's lead author.

The study was notable not only for its size—unusual for ME/CFS/SEID research—but also for the meticulousness of its design. The study was funded by the Chronic Fatigue Initiative of the Hutchins Family Foundation, which worked with expert clinicians who understand how to diagnose ME/CFS and to enroll well-characterized patients.

Hornig says that she and her colleagues plan to replicate the results in a year-long longitudinal study that tracks patients' cytokine levels over time. One particular cytokine of interest is interleukin-17A, which was shown to be elevated in early-stage patients in the study.

The second Hornig-Lipkin study corroborates the findings of the first. In the study released March 31, researchers again employed immunoassay testing methods to measure the levels of 51 cytokines in the cerebrospinal fluid of

Dr. Mady Hornig is the study's lead author.

32 patients who had ME/CFS/SEID for an average of seven years, 40 patients who had multiple sclerosis and 19 non-diseased controls. The researchers found that the levels of most cytokines—including interleukin 1—were depressed in the ME/CFS patient group, compared with the other two groups. These results are similar to what was found in ME/CFS/SEID patients of more than three years from the earlier study.

"We now know that the same changes to the immune system that we recently reported in the blood of people with ME/CFS with long-standing disease are also present in the central nervous system," said Hornig. "These immune findings may contribute to symptoms in both the peripheral parts of the body and the brain from muscle weakness to brain fog." ■

Building Momentum

Throughout this issue of the *SolveCFS Chronicle*, we have shared important information on how the momentum is building for ME/CFS/SEID. From the landmark IOM report and our Washington, D.C., briefing urging more research funding, to new publications coming out of the work through the SolveCFS BioBank™, to our half million dollar study on epigenetics and more, we are at a tipping point for real progress.

While we're pleased to see this momentum building, we know so much more needs to be done. We must continue funding researchers through the SolveCFS BioBank™, fostering innovation, collaboration and progress among the best and the brightest. We must urge the federal government to provide funding for research commensurate with the disease burden to eradicate this dreadful disease once and for all. Until ME/CFS/SEID is understood, diagnosable and treatable, until there is a cure, we will remain vigilant in our fight to Solve ME/CFS.

But we cannot do this alone. You can help us continue this important momentum. We count on the gifts of individuals just like you to fund progress. There are many ways to give…

- ✓ Join our Sustainers Circle by becoming a regular, monthly donor at SolveCFS.org/donate. If you already are a monthly donor, consider increasing your gift by 10 percent to 25 percent. These regular, monthly gifts, regardless of the size, steadfastly support our important work year-round.
- ✓ Join "Team Solve" by creating your own fundraising campaign for ME/CFS/SEID research on Crowdrise at www.Crowdrise.com/SolveCFS. You can set up your own personal web page and invite family and friends to join you in making a difference for all who suffer. If this interests you, we'd love to talk to you about it. Contact Leigh Reynolds at LAReynolds@SolveCFS.org or call 704-364-0016.
- ✓ Take advantage of workplace giving. Ask if your employer has a matching gift program, which could double any donation. Or write in the Solve ME/CFS Initiative as your "charity of choice" for the United Way or Independent Corporate Campaign. We also participate in federal and state employee giving programs.

The road to real discovery and life-changing progress is long, arduous and costly. The Solve ME/CFS Initiative is taking strategic steps to shorten the road and speed up progress. Despite our modest budget, SMCI was the first organization to fund research into epidemiology, viral causes, immunology, neuroimaging, exercise physiology and the autonomic nervous system.

All of this research work is only possible because of the support of the many who fund it. The investments made by those suffering with ME/CFS and their loved ones have fueled the Solve ME/CFS Initiative's work. We're all in this together.

To join the vital community fighting ME/CFS/SEID through gifts to SMCI, please visit www.solvecfs.org/donate or send a tax-deductible donation to: Solve ME/CFS Initiative, P.O. Box 36007; Los Angeles, Calif. 90036-0007 using the envelope included in this publication.

I Am Bent But Not Broken (continued from Page 1)

5 percent to 30 percent. Additional visits to BioCare Hospital, as well as major lifestyle and dietary adjustments, eventually increased my functionality to 75 percent.

While I began to see physical improvements, I sought additional resources for emotional and financial relief. I set out on a mission to find patient/caregiver-focused groups that offered the kind of assistance I was in need of and much to my dismay, my search left me empty-handed. That is, until I decided to put my 15-year journey with ME/CFS to use and founded Bent But Not Broken.

In 2012, I founded Bent But Not Broken in an effort to provide emotional, educational and financial resources to patients and their caregivers living with ME/CFS. With a focus on helping patients with their immediate needs, BBNB's board members and I developed a financial application that patients or caregivers can fill out to request monetary support of treatments, tests and health management tools that are not covered by insurance companies or state and federal assistance programs. To date, BBNB has received over $1.2 million in funding requests. These requests are funded strictly from online and event donations.

To provide emotional and educational assistance, I began posting my own personal experiences and findings in an active blog, which is accessible through BBNB's website. The website, along with social media sites, provide the ME/CFS community with product reviews, resource listings and industry news about ME/CFS.

The community surrounding me has been incredibly supportive and has allowed BBNB to grow to a 10-person volunteer board. In recent months, BBNB was given the opportunity to partner with organizations such as the Solve ME/CFS Initiative, Script Relief and Co-Patient to further the information and resources we offer patients. My goal is to eventually link all ME/CFS communities involving research, advocacy, awareness, financial assistance, emotional support, legal advice and more, to provide patients with a one-stop shop for the best possible resources.

Looking to the future, my only hope is that my story will encourage others to persevere. Now, what used to feel like 50 percent actually feels like 90 percent thanks to the positivity BBNB has brought to my life. It has given me things that ME/CFS/SEID can never take away: passion to help, wisdom to inspire and courage to live. I want others to feel that, too, because we are all just bent, not broken. ■

Bent But Not Broken

bentbutnotbroken.org

Lindsey Beres, ME/CFS/SEID patient and founder of Bent But Not Broken

Spread the Word!

If you're already signed up for our weekly blog, monthly e-newsletter and webinar series, let a friend or family member know, too:

SolveCFS.org/blog

SolveCFS.org/Research1st

SolveCFS.org/webinar

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International ME/CFS Awareness Day — May 12

On Tuesday, May 12, patients and their loved ones from across the globe came together to help spread awareness of and compassion for ME/CFS.

While May 12 has passed, this effort will be effective throughout the month of May and beyond, so let's keep the momentum going! Please visit our **May 12 Awareness Day** page at SolveCFS.org/May12, find a way to participate that is meaningful to you, and join us as we continue to make ME/CFS more understood.

Each of us on our own can only do so much, but when we raise our voices together, we can be heard. We can make a difference. We can change the world for the millions who suffer from ME/CFS.

Stay in touch!

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